REMARKS

Claims 1, 8 and 33-54 are currently pending. New claims 55 to 63 have been added. Support for the new claims can be found throughout the specification; for example, support for new claim 55 can be found at least at page 22, lines 16-17; and page 23, lines 7-8. Support for new claims 56-58 can be found at least at page 7, line 8. Support for new claims 59-61 can be found at least at page 7, lines 17-22; page 14, lines 12-25; and in Example 1. Support for claim 62 can be found at page 2, lines 12-14; and in Table 1. Support for claim 63 can be found at least at page 14, lines 28-31. Support for the amendment of claims 8, 34-36 and 43-46 can be found at least at page 5, lines 13-15; and page 7, lines 17-20. Support for the amendment of claims 1, 8, 34-41, 43-46, 52 and 53 can be found at least at page 11, lines 2-7; and page 6, lines 4-13. Claim 8 was also amended to insert the word "intake." Claims 33, 47, 51 and 54 were amended to be dependent on the newly added claims. Claims 2-7 and 9-32 were previously canceled without prejudice or disclaimer. No new matter has been introduced. Upon entry of the present amendment, claims 1, 8, and 33-63 will be pending.[2]

Rejections Under 35 U.S.C. § 112, First Paragraph – Enablement

The rejection in the Office Action of November 30, 2004 of claims 1, 8 and 33-54 under 35 U.S.C. § 112, first paragraph as allegedly lacking enablement was maintained. The Examiner notes that claims 8, 33-36, 43-52 and 54 were not amended to recite peripheral administration. Applicants have amended claims 8, 34-36, and 43-46 to recite peripheral administration, claims 33, 47-52 and 54 depend from the amended claims, and the rejection is hereby overcome.

The Examiner alleges that "the claims are drawn to a method comprising administration of a genus of structurally undefined PYY agonists," and that "the disclosure cannot reasonably provide enablement for the genus of PYY agonists without enabling its species" (Final Office Action mailed June 29, 2005; pages 4 and 6, respectively). Applicants respectfully disagree with this rejection. However, without

2. Applicants wish to bring to the Examiner's attention co-pending U.S. applications 10/518,128, 11/055,098, assigned to Amylin Pharmaceuticals, Inc., and applications 09/499,526 and 10/855,676, licensed to Amylin Pharmaceuticals, Inc.

acquiescence to the rejection and solely to advance prosecution, Applicants have amended claims 1, 8, 34-41, 43-46, 52 and 53 to recite "wherein the PYY agonist is a peptide."

Applicants note that PYY agonists are set forth in the specification. For example, SEQ ID NO. 2 sets forth the sequence of PYY, and SEQ ID NO. 3 sets forth the sequence of PYY[3-36]. Additionally, PYY agonists are provided in Table 1, on page 10, and are defined at least on page 5, lines 24 through page 6, line 19 and page 19, lines 6-8. Furthermore, other PYY agonists were known in the art at the time of filing.[3] The specification provides methods for determining whether a PYY agonist is effective in reducing food intake (Example 1), body weight (Example 6), and/or caloric efficiency (Example 7). Examples 9 and 10 are directed to methods of evaluating PYY agonist activity using the area postrema assay and the Y receptor binding assay. These assays are routine for the skilled artisan, not requiring undue experimentation, and the Patent Office has provided no objective evidence that such methods would not work.

It appears that the Examiner is arguing that, while PYY agonists were known in the art at the time of filing, these agonists were used for different purposes. This argument, however, is insufficient to support a lack of enablement rejection because the cited references are not necessary to teach how to make and use the claimed invention. To the contrary, Applicants specification provides specific teachings of how PYY agonists can be used in the claimed methods; whatever the purposes allegedly taught by the cited U.S. patents, the PYY agonists themselves were known in the art, and assays for determining their effectiveness in the novel methods of the instant invention are set forth in the specification as filed.

Moreover, the Office has not satisfied its burden of challenging Applicants' presumptively correct assertion that the invention is enabled (M.P.E.P. § 2164.04). As stated in the M.P.E.P:

> A specification disclosure which contains a teaching of the manner and process of making and using an invention in terms which correspond in scope to those used in describing and defining the subject matter sought to be patented must be taken as being in compliance with the enablement requirement of 35

3. See, for example, U.S. Patent 5,574,010; U.S. patent 5,696,093; and U.S. Patent 5,604,203.

> U.S.C. 122, first paragraph, unless there is a reason to doubt the objective truth of the statements contained therein which must be relied on for enabling support.

If sufficient reason for such doubt exists, "it is incumbent upon the Patent Office, whenever a rejection on this basis is made, to explain *why* it doubts the truth or accuracy of any statement in a supporting disclosure and to back up assertions of its own with acceptable evidence or reasoning which is inconsistent with the contested statement." *In re Marzocchi*, 439 F.2d 220, 224, (CCPA 1971) (emphasis in original). Furthermore, this standard is applicable even when there is no evidence in the record of operability without undue experimentation beyond the disclosed embodiments. *In re Bowen*, 492 F.2d 859, 862-63, (CCPA 1974).

Applicants provided enabling description of PYY, PYY agonists and PYY agonist analogs. The specification as filed sets forth PYY and PYY agonists and cites references describing known PYY agonists and PYY agonist analogs. The specification sets forth assays for determining whether a PYY agonist or PYY agonist analog is effective in the claimed methods and sets forth evidence that PYY agonists do function as claimed. The Office has provided no objective evidence that the known PYY agonists or PYY agonist analogs would not function in the methods as claimed. Nonetheless, and without agreeing to the rejection, Applicants have amended the claims to recite peptidyl PYY agonists. Applicants respectfully request reconsideration and withdrawal of the rejection of claims 1, 8, 33-50 and 52-54 for lack of enablement.

Rejections Under 35 U.S.C. § 112, First Paragraph – Written Description

The rejection in the Office Action of November 30, 2004 of claims 1, 8, 33-46 and 48-54 under 35 U.S.C. § 112, first paragraph as allegedly lacking written description was maintained. The Examiner alleges "the claims are drawn to a method comprising administration of a genus of structurally undefined PYY agonists" (Final Office Action mailed June 29, 2005; page 8). Applicants disagree. However, to expedite prosecution, Applicants have amended claims 1, 8, 34-41, 43-46, 52 and 53 to recite "wherein the PYY agonist is a peptide."

As discussed herein, SEQ ID NO. 2 and SEQ ID NO. 3 set forth PYY and PYY[3-36], respectively. Additional PYY agonists and PYY agonist analogs are

described in the specification and cited references, and assays are set forth for determining whether a PYY agonist or PYY agonist analog is effective in the claimed methods. The courts have ruled that, to meet the written description requirement, an Applicant is not required to re-describe that which is already known or readily determined by known procedures. See *Capon v. Eshhar*, 418 F.3d 1349 (Fed. Cir., 2005). Applicants respectfully submit that the skilled artisan would readily recognize that the Applicants were in possession of the claimed invention. Applicants, therefore, respectfully request reconsideration and withdrawal of the rejection of claims 1, 8, 33-46 and 48-54 under 35 U.S.C. § 112, first paragraph.

Rejections Under 35 U.S.C. § 112, Second Paragraph – Indefiniteness

Claims 1, 8, 33-42 and 47-54 were rejected under 35 U.S.C. § 112, second paragraph, as allegedly being indefinite for failing to particularly point out and distinctly claim the subject matter which applicants regard as the invention. In particular, with respect to the phrase "desirous of reducing caloric efficiency," the Examiner alleges that "(i)t is unclear how such a limitation, which represents a mental process, limits the subject recited in the claims" (Final Office Action mailed June 29, 2005; page 10). Applicants respectfully disagree.

The proper test of indefiniteness is whether one of ordinary skill in the art would understand what is claimed. "If the claims, read in the light of the specification, reasonably apprise those skilled in the art both of the utilization and scope of the invention, and if the language is as precise as the subject matter permits, the courts can demand no more." *Georgia-Pacific Corp. v. United States Plywood Corp.*, 258 F.2d 124, 136, 132 (2d Cir, 1958).

The phrase "a subject desirous of" is not indefinite. Applicants disagree with the Examiner's contention that this phrase "represents a mental process" and that "(i)t is unclear how such a mental process limits the subject population." The Examiner has failed to give any reasoning why a person of ordinary skill would not understand what is meant by the phrase "a subject desirous of." For example, page 6, lines 28-30 of the specification describes "any subject ...who needs or wishes to reduce body weight," and page 14, lines 19-22 states "Administration should begin whenever the suppression of

nutrient availability, food intake, weight, blood glucose or plasma lipid lowering is desired, for example, at the first sign of symptoms or shortly after diagnosis of obesity, diabetes mellitus, or insulin resistance syndrome." When reading the claims in light of the specification, the skilled artisan would have no difficulty interpreting this language.[4] Applicants respectfully request reconsideration and withdrawal of these rejections under 35 U.S.C. § 112, second paragraph.

Rejections Under 35 U.S.C. § 102(b)

The rejection in the Office Action of November 30, 2004 of claims 1, 8, 33-42, 47-49 and 52-54 under 35 U.S.C. § 102(b) as allegedly being anticipated by Yoshinaga, et al., (*Am. J. Physiol.* 263:G695-701, 1992) was maintained. The Examiner alleges that the method of inhibiting pancreatic exocrine secretion and gastric acid output in dogs of Yoshinaga are "necessarily liked to other properties of PYY or PYY agonists such as caloric efficiency, nutrient availability, appetite, food intake, or weight" and that "the intended uses and properties of the PYY or PYY agonist recited in the claims are inherent to the method taught by Yoshinaga" (Final Office Action mailed June 29, 2005, page 11). Applicants respectfully traverse the rejection, because Yoshinaga does not teach, expressly or inherently, each element recited in the claims.

Whatever Yoshinaga does teach with regard to inhibition of gastric acid and pancreatic exocrine secretion, it fails to disclose or even contemplate a method of administering an amount of PYY or PYY agonist effective to reduce caloric efficiency, nutrient availability, appetite, food intake, body weight or body weight gain, or increase weight loss. The claimed methods require administration of an amount of a PYY or a PYY agonist effective to reduce caloric efficiency, nutrient availability, appetite, food intake, body weight or body weight gain, or increase weight loss. The effectiveness of a PYY or PYY agonist on reducing caloric efficiency, nutrient availability, appetite, food intake, body weight or body weight gain, or increasing weight loss was not measured in the dogs of Yoshinaga.

4. Applicants note that the Patent Office has issued patents with claims containing this language (see US Patents 5,890,492 and 5,899,502), and at least one court has ruled that the use of the word "desired" in a claim leads to no ambiguity. *Biomeridian Intern., Inc. v. Clark*, 2003 WL 23354485, (D. Utah).

It appears that the Examiner has taken two complex physiologic responses and linked them without presenting any evidence that they are absolutely and always linked. It is illustrative to consider page G698 of Yoshinaga, which states that PYY[3-36] "showed biological activities in the pancreatic insulin and gastric acid bioassays that were significantly less than" full length PYY, while no difference was observed between the two peptides with respect to the inhibition of pancreatic secretion. However, Applicants' own data show that the effectiveness of PYY[3-36] is greater than or equal to that of full length PYY in the food intake and gastric emptying assays (see Table 1). Thus, it cannot be assumed that the inhibition of gastric acid and pancreatic exocrine secretion of Yoshinaga are necessarily and always linked to the reduction in nutrient availability, caloric efficiency, food intake and/or body weight of the instant invention.

Moreover, Yoshinaga cannot render unpatentable by inherency the subject population of claims 1, 8, 33-42, 47-54 and new claims 56-62, i.e., subjects desirous or in need of reducing caloric efficiency, nutrient availability, body weight, food intake or appetite. Additionally, Yoshinaga does not anticipate the human subjects of claims 44-46 and new claim 63. Neither does Yoshinaga anticipate the use of PYY agonists with the binding profile of claims 38-42, 53 and 62. Finally, Yoshinaga does not anticipate reducing food intake of claims 34, 39, 43, 44 and 56, nor reducing non-high fat food intake of claims 8 and 35, nor reducing intake of or appetite for food which comprises both high and low fat food of claims 34 and 36, nor reducing appetite of claims 35, 36, 40, 45, 46 and 57, nor reducing weight, weight gain or increasing weight loss of claims 52, 53, or 55.

Because the disclosure of Yoshinaga does not teach, expressly or inherently, each element recited in the claims, the 102(b) rejection is improper. Applicants respectfully request reconsideration and withdrawal of the rejection of claims 1, 8, 33-42, 47-49 and 52-54 under 35 U.S.C. § 102(b).

The rejection in the Office Action of November 30, 2004 of claims 1, 33, 38, 42, 48-50 and 52-54 under 35 U.S.C. § 102(b) as being allegedly anticipated by Morley, et al., (*Life Sci.* 41:2157-2165, 1987) was maintained. Applicants respectfully traverse this

rejection, because Morley does not teach, expressly or inherently, each element recited in the claims.

Specifically, Morley does not teach that administration of a PYY or PYY agonist reduces food intake as required by claims 34, 39, 43, 44 and 56. In fact, Morley expressly teaches that "peripherally, PYY caused weight loss, without altering food intake" (page 2164). In contrast, Example 1 of the instant invention demonstrates that peripherally administered PYY or PYY agonist significantly reduces food intake. Because Applicants have shown that peripheral administration of PYY reduces food intake, the experiments in Morley may be considered "failed experiments." The courts have ruled that a failed experiment reported in a reference renders that reference irrelevant as a prior art reference.[5]

Additionally, there is no indication in Morley that the murine subjects of the experiments were obese. Morley does not anticipate the subject population of claims 1, 8, 33-42, 47-54 and new claims 56-62, i.e., subjects desirous or in need of reducing caloric efficiency, nutrient availability, body weight, weight gain, food intake or appetite, or increasing weight loss. Neither does Morley anticipate the human subjects of claims 44-46 and new claim 63. Morley does not teach or even suggest methods of reducing non-high fat food intake of claims 8 and 35, nor reducing appetite of claims 34, 35, 36, 40, 45, 46 and 57. Neither does Morley teach, expressly or inherently, the use of PYY agonists with the binding profile of claims 38-42, 53 and 62, or the use of PYY[3-36] of claim 47. Applicants respectfully request reconsideration and withdrawal of the rejection of claims 1, 33, 38, 42, 48-50 and 52-54 under 35 U.S.C. § 102(b).

The Examiner has rejected claims 1, 8, 33-42, 47-50 and 52-54 under 35 U.S.C. § 102(b) as being allegedly anticipated by Okada, et al., (The Endocrine Society 75th Annual Meeting Program & Abstract, page 180, Abstract 520B, 1993). Applicants respectfully traverse the rejection, because Okada does not teach, expressly or inherently, each element recited in the claims.

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5. As stated by Judge Learned Hand, "another's experiment, imperfect and never perfected will not serve either as an anticipation or as part of the prior art, for it has not served to enrich it." *Picard v. United Aircraft Corp.*, 128 F.2d 632, 635, 53 USPQ 563, 566 (2d Cir.1942), *cert. denied,* 317 U.S. 651, 63 S.Ct. 46, 87 L.Ed. 524 (1942).

The Examiner alleges "all the intended uses and properties of the PYY and PYY agonist recited in the claims are inherent to the method taught by Okada, et al." Okada discusses an experiment in which rats on a high fat diet were peripherally administered PYY and a reduction in food intake was observed. Okada does not teach, expressly or inherently, reducing intake of or appetite for food which comprises both high and low fat food of claims 34 and 36, nor does it teach reducing intake of or appetite for non-high fat food of claims 8 and 35. Okada does not teach or suggest the human subjects of claims 44-46 and 63, and cannot anticipate, expressly or inherently, the claimed subject population, i.e., subjects desirous or in need of reducing caloric efficiency, nutrient availability, weight, weight gain, food intake or appetite, or increasing weight loss of claims 1, 33, 37, 47-50, 52 and 54. Neither does Okada teach PYY[3-36] of claim 47. Okada mentions only PYY, which does not have the binding profile set forth in claims 38-42, 53 and 62.

When making a rejection "relying upon the theory of inherency, the examiner must provide a basis in fact and/or technical reasoning to reasonably support the determination that the allegedly inherent characteristic necessarily flows from the teachings of the applied prior art." *Ex parte Levy*, 17 USPQ2d 1461, 1464 (Bd. Pat. App. & Inter. 1990). The Examiner has made no attempt to establish inherency by a showing of extrinsic evidence that "the missing descriptive matter is necessarily present in the thing described in the reference" *Continental Can Co. v Monsanto Co.*, 948 F2d 1264; 20 USPQ2d 1749 (Fed. Cir. 1991). The Examiner has provided no basis in fact and/or technical reasoning to support the contention that the claims of the instant invention necessarily flow from the observed reduction in high-fat food intake observed in rats peripherally administered PYY reported by Okada. The methods of the claimed invention cannot be assumed to be the natural result flowing from the reduction in high-fat food intake as taught. "Inherency ... may not be established by probabilities or possibilities. The mere fact that a certain thing may result from a given set of circumstances is not sufficient" *Hansgirg v. Kemmer*, 26 CCPA 937, 940, 102 F.2d 212, 214, 40 USPQ 665, 667 (1939).

Because the examiner has not established that each element required by the claims is expressly or inherently anticipated by Okada, Applicants respectfully submit

that the 102(b) rejection is improper. Applicants respectfully request reconsideration and withdrawal of the rejection of claims 1, 8, 33-42, 47-50 and 52-54 under 35 U.S.C. § 102(b).

Rejections Under 35 U.S.C. § 103(a)

The rejection of claim 51 under 35 U.S.C. § 103(a) as being allegedly unpatentable over Okada in view of Naslund, et al. (*Int. J. Obes. Relat. Metab. Disord.* 23:304-311, 1999) in the Office Action of November 30, 2004 was maintained. Applicants respectfully request withdrawal of this rejection, because the Examiner has not established a *prima facie* case of obviousness.

In establishing a *prima facie* case of obviousness under 35 U.S.C. § 103, there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify a primary reference or to combine reference teachings. "Both the suggestion and the reasonable expectation of success must be found in the prior art, not in the applicant's disclosure." *In re Vaeck*, 947 F.2d 488, 493 (Fed. Cir. 1991). It is incumbent upon the Examiner to provide a reason why one of ordinary skill in the art would have been led to modify a prior art reference or to combine reference teachings to arrive at the claimed invention. *Ex parte Clapp*, 227 U.S.P.Q. 972 (Bd. Pat. App. Int. 1985). The mere possibility that the prior art can be modified, however, does not itself provide the requisite motivation to do so. *In re Dien*, 152 U.S.P.Q. 550 (C.C.P.A. 1967). Only when the prior art teaches or suggests the claimed invention does the burden fall on the applicant to rebut that *prima facie* case. *In re Dillon*, 919 F.2d 688, 692, (Fed. Cir. 1990).

Claim 51 claims a method of peripheral administration of a PYY or a PYY agonist "further comprising administration of a GLP-1, an exendin, an amylin, their agonists, or any combination thereof." Okada observes a decrease in high-fat food intake in rats. For the reasons set forth above, Okada does not teach or suggest all the limitations of the claimed invention. Okada fails to teach GLP-1, an exendin, an amylin, their agonists, or any combination thereof, and does not teach the co-administration of a PYY or a PYY agonist with any other compound. Naslund does not cure the deficiencies of Okada. Naslund reports the administration of GLP-1 alone, and merely states that

"(b)lood samples were obtained for the analysis of plasma concentrations of insulin, C-peptide, GLP-1 and peptide YY" (page 305). In other words, Naslund teaches measurement of endogenous PYY, and does not teach or suggest administration of exogenous PYY, PYY agonists, exendin, amylin, their agonists, or any combination thereof, nor does it teach co-administration of GLP-1 with any other compound. Neither Naslund nor Okada teaches or suggests the combination, and the Examiner's conclusory statement that the combination would be obvious is not evidence of sufficient motivation to impel the skilled artisan to do what Applicants have done. The Federal Circuit court has ruled that "(b)road conclusory statements regarding the teaching of multiple references standing alone are not 'evidence.'" *In re Dembiczak*, 175 F.3d 994, 999 (Fed. Cir. 1999).

The Examiner has pointed to nothing in the cited references or the art to suggest their combination. Even if combined, the Examiner has pointed to nothing to suggest the modifications of the references needed to meet all of the limitations of the present claims. Therefore, Applicants respectfully request reconsideration and withdrawal of the rejection of claim 51 under 35 U.S.C. § 103(a).

The rejection of claim 51 under 35 U.S.C. § 103(a) as being allegedly unpatentable over Morley in view of Naslund in the Office Action of November 30, 2004 was maintained. Applicants respectfully traverse the rejection, as the references do not teach or suggest all the claim limitations.

As discussed above, Morley teaches away from the peripheral administration of a PYY or a PYY agonist as a method of reducing food intake. Teaching away is the very antithesis of obviousness. *In re Buehler* 515 F.2d, 1134 (CCPA 1975). Morley does not teach or suggest methods of reducing caloric efficiency, appetite or nutrient availability, or the administration of PYY in combination with a GLP-1, an exendin, an amylin, their agonists, or any combination thereof." The deficiencies of Morley are not cured by the addition of Naslund, because Naslund teaches measurement of endogenous PYY, and does not teach or suggest 1) administration of an exogenous PYY or PYY agonist, 2) administration of GLP-1 with any other compound, or 3) an exendin, an amylin, their agonists, or any combination thereof.

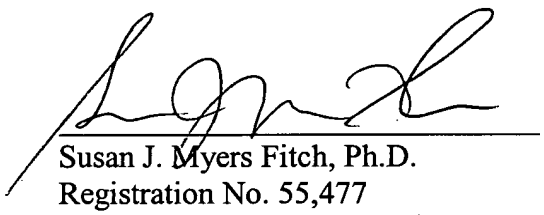
The Examiner has pointed to nothing in the cited references or in the art to suggest their combination. Even if combined, the Examiner has pointed to nothing to suggest the modification of the references needed to meet all of the limitations of the present claims. Therefore, Applicants respectfully request reconsideration and withdrawal of the rejection of claim 51 under 35 U.S.C. § 103(a).

Conclusion

In light of the foregoing amendments and remarks, Applicants respectfully request reconsideration and withdrawal of all objections and rejections set forth in the Final Office Action of June 29, 2005. Further, Applicants believe all claims presently under consideration to be in a condition for allowance and request issuance of a Notice of Allowance at the Examiner's earliest convenience.

Should the Examiner have any remaining questions regarding the subject invention or its patentability, Applicants encourage the Examiner to contact the undersigned to discuss any issues remaining.

Respectfully submitted,



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